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March 28, 1938.

Dr. Max Delbruck,
California Institute of Technology,
Pasadena, Cal.

Dear Dr. Delbruck:

I wish I could attend the seminar you and Dr. Pauling are planning to run, although I fear my physical background would not be adequate.

Under separate cover I am sending copies of the reprints which we still have, including the precipitin theory. I should be glad to have you return this one when you have finished it. I am also sending the derivation of the three-stage equation, although it does not have to be used in practice.

I am very glad that you are both interested in serological specificity and its mechanisms and hope you will emerge with something more satisfactory than our makeshift. I think your theory of reaction velocity a plausible one, and some actual diffusion constants will be published very shortly by Kabat and Pedersen in "Science", so that you may be able to use them. I do not know, though, how you will be able to distinguish between the primary union of multivalent antigen and multivalent antibody and the subsequent unions which build up the large aggregates which ultimately separate. I imagine the velocity must decrease greatly as the aggregate increases in size. Can you provide for a constantly diminishing collision rate? Also, in the precipitin reaction between pneumococcus polysaccharides and potent antisera visible reaction takes place almost instantly except at high dilutions and in the cold, so that there is no obvious difference between the large horse and small rabbit antibody molecules. It is also known that the velocity of precipitation is greatly influenced by the pH , so that all of these effects must be taken into account in a completely satisfactory theory.

Velocity of combination has been discussed by (), and by Hooker and Boyd (J.Bact.:36,31,69,57,33,70; J.Gen.Physiol.:35,19,373; J. Immunol.:37,33,337), but velocity of particulation was actually measured. Eagle has also published some data which could be explained on almost any theory (J.Immunol.:50,18,593).

Our theories have been attacked by Malkiel and Boyd (J.Exp.Med.:37,66,383), apparently as a result of a complete misapprehension as to the range covered by our antibody excess equation, and by Hooker and Boyd (J.Immunol.:37,33,337), partly because they failed to note that

the conditions of the experiment criticized eliminated the alternative they suggest, and partly on the basis of their own experiments, the technique and subject matter of which are, I believe, open to some objection.

Wishing you all success, and looking forward eagerly to the result of your deliberations,

Sincerely,

Michael Heidelberger.